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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/338,855	06/23/99	SORGE J	04435/79243

EXAMINER	
CHAKRABARTI, A	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/338,855	Sorge
Examiner	**Group Art Unit**
Arun Chakrabarti	1655

☒ *Responsive to communication(s) filed on* Feb 12, 2001 .

☐ *This action is* **FINAL.**

☐ *Since this application is in condition for allowance except for formal matters,* **prosecution as to the merits is closed** *in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.*

A shortened statutory period for response to this action is set to expire 3 *month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).*

Disposition of Claims

☒ *Claim(s)* 1-3, 57-74, and 145-156 *is/are pending in the application.*

Of the above, claim(s) _____ *is/are withdrawn from consideration.*

☐ *Claim(s)* _____ *is/are allowed.*

☒ *Claim(s)* 1-3, 57-74, and 145-156 *is/are rejected.*

☐ *Claim(s)* _____ *is/are objected to.*

☐ *Claims* _____ *are subject to restriction or election requirement.*

Application Papers

☐ *See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.*

☐ *The drawing(s) filed on* _____ *is/are objected to by the Examiner.*

☐ *The proposed drawing correction, filed on* _____ *is* ☐*approved* ☐*disapproved.*

☐ *The specification is objected to by the Examiner.*

☐ *The oath or declaration is objected to by the Examiner.*

Priority under 35 U.S.C. § 119

☐ *Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).*

☐ *All* ☐ *Some** ☐ *None of the CERTIFIED copies of the priority documents have been*

☐ *received.*

☐ *received in Application No. (Series Code/Serial Number)* _____ .

☐ *received in this national stage application from the International Bureau (PCT Rule 17.2(a)).*

**Certified copies not received:* _____ .

☐ *Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).*

Attachment(s)

☒ *Notice of References Cited, PTO-892*

☒ *Information Disclosure Statement(s), PTO-1449, Paper No(s).* 4 and 6

☐ *Interview Summary, PTO-413*

☐ *Notice of Draftsperson's Patent Drawing Review, PTO-948*

☐ *Notice of Informal Patent Application, PTO-152*

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant has elected Group I corresponding to claims 1-3 with traverse. Applicant's election with traverse of Group I in Paper No. 7 is acknowledged. The traversal is on the ground(s) that reconsideration of the restriction requirement as to the claims 57-74 is requested. This traversal has been found persuasive and therefore claims 57-74 are hereby being examined. New claims 145-156 have been added.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-3 , 57-74 and 145-156 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-3 , 57-74 and 145-156 are rejected as indefinite because the instantly claimed method lacks a final process step that clearly relates back to the preamble. For the method of claim 1, the preamble of the instantly claimed method is drawn to a method of enriching for and identifying a nucleic acid sequence difference while the final process step is that of detecting a sequence difference only and it is thus unclear as to whether the instantly claimed method is drawn to a method of enriching for and identifying a nucleic acid sequence difference or rather detecting a sequence difference only. Method claim requires a last

step or phrase in the last step that states the accomplishments of the goals for the method which were stated in the method's preamble.

Similarly, for the method of claims 57 and 69, the preamble of the instantly claimed method is drawn to a method of enriching for and identifying a nucleic acid sequence difference while the final process step is that of detecting a sequence difference only and it is thus unclear as to whether the instantly claimed method is drawn to a method of enriching for and identifying a nucleic acid sequence difference or rather detecting a sequence difference only. Method claim requires a last step or phrase in the last step that states the accomplishments of the goals for the method which were stated in the method's preamble. Method claim requires a last step or phrase in the last step that states the accomplishments of the goals for the method which were stated in the method's preamble

Claims 1, 57 and 69 lack such a last step and are confusing because the additional method step is not sufficiently set forth. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashions. See Ex parte Erlich, 3 USPQ2d1011, p.1011 (Bd. Pat. Applicant. Int. 1986). It is suggested that an amended claim more clearly describing the intended steps be submitted.

Claims 57-74 are also rejected over the recitation of the phrase, "capable of". Regarding claims 57 and 69, the phrase "capable of" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 155-156 are rejected over the recitation of the phrase, "infrequently". It is not clear what kind of infrequency is claimed in this invention. The use of a particular restriction endonuclease depends on the specific sequence of the nucleic acid to be cleaved and the subsequent use of the cleaved nucleic acid for a particular purpose. In view of this fact and in view of the absence of a particular nucleic acid sequence presented in the claim, the term "infrequently" is relative, vague and indefinite. The metes and bounds of the claims are vague and indefinite.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 1-3, 57-74 and 150-153 are rejected under 35 U.S.C. 102 (a) as being anticipated by Oefner et al. (U.S. Patent 5,795,976) (August 18, 1998).

Oefner et al. teach a method of enriching for and identifying a nucleic acid sequence difference with respect to a reference sequence and a method for accessing a sub-portion of a nucleic acid population (Abstract), comprising:

a) hybridizing a nucleic acid sample with a nucleic acid molecule comprising a sequence-specific binding activity under conditions which permit specific binding, wherein the sample comprises a subset of nucleic acid molecules having a sequence that binds to the sequence-

specific binding activity, and wherein a bound subset of nucleic acid molecules is retained by the sequence-specific binding activity, such that the subset of bound nucleic acid molecules is enriched for molecules comprising the sequence recognized by the sequence specific binding activity (Column 9, lines 39-43, Example 2 and Column 13, line 21 to column 17, line 12); and

b) detecting a sequence difference with respect to a reference sequence in the subset of nucleic acid molecules (Column 18, lines 1-30 and Example 7, column 34, lines 7-13, Example 8, column 34, line 53 to column 36, line 27 and Figures 11A and 11B).

Oefner et al. teach a method wherein the molecule comprising sequence-specific binding activity is selected from nucleic acid molecules (Abstract, Column 22, line 59 to Column 24, line 58).

Oefner et al. teach a method wherein the sequence-specific binding activity is bound to a solid support (Examples 2, 3, 4, 5, 6 and 8 and Figures 1-4 and 6-13).

Oefner et al. teach a method of enriching for and identifying a nucleic acid sequence difference with respect to a reference sequence (Abstract), comprising:

a) fragmenting a nucleic acid sample from one or more individuals (Column 9, lines 39-43);

b) physically separating a subset of the nucleic acid fragments based on the size of the fragments (Example 2 and Column 13, line 21 to column 17, line 12);

c) operatively linking the subset of step (b) with molecules capable of being replicated (Column 13, line 21 to column 17, line 12);

d) introducing the linked subset of molecules of step c) into a system capable of replicating the linked subset of molecules, and replicating the subset of linked molecules to form an enriched collection of replicated molecules (Column 17, lines 14-67).

e) detecting one or more nucleotide sequence differences in the members of the collection of step (d) with a method capable of detecting one or more nucleotide differences with respect to a reference sequence (Column 18, lines 1-30 and Example 7, column 34, lines 7-13, Example 8, column 34, line 53 to column 36, line 27 and Figures 11A and 11B).

Oefner et al. teach a method wherein the system capable of replicating the linked molecules comprises host cells and the collection of replicated molecules comprises a library (Column 22, line 59 to Column 24, line 58).

Oefner et al. teach a method wherein the system capable of detecting one or more nucleotide conformational differences comprises DNA sequencing by electrophoresis (Column 35, lines 3-27).

Oefner et al. teach a method wherein the method capable of detecting one or more nucleotide difference comprises denaturing HPLC (Examples 2, 3, 4, 5, 6 and 8 and Figures 1-4 and 6-13).

Oefner et al. teach a method wherein the method capable of detecting one or more nucleotide difference comprises a protein capable of detecting mismatches between duplexed strands of nucleic acid (Column 23, lines 45-56).

Oefner et al. teach a method wherein the steps (a)- (b) are repeated one or more times to increase the enrichment of the enriched collection of repeated molecules (Example 7).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-3, 57-74, and 145-155 are rejected under 35 U.S.C. 103 (a) over Oefner et al. (U.S. Patent 5,795,976) (August 18, 1998) in view of Bloch et al (U.S. Patent 5,866,429) (February 2, 1999) .

Oefner et al teach the method of claims 1-3, 57-74 and 150-153 as described above.

Oefner et al do not teach the fragmenting a nucleic acid sample by endonuclease digestion.

Bloch et al teach the fragmenting a nucleic acid sample by restriction endonuclease digestion (Example 1, column 19, lines 58-64).

Bloch et al teach the fragmenting a nucleic acid sample with one or more sequence - specific cleavage agents restriction endonuclease to produce nucleic acid fragments (Example 1, column 19, lines 58-64). Bloch et al teach the method wherein at least one restriction endonuclease cleaves DNA infrequently (Example 4, column 24, lines 5-8).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine within the method of comparative hybridization and sequencing of Oefner et al., the method of restriction endonuclease digestion of Bloch et al. since Bloch et al state, "Another preferred method, used alone or together with PCR, for providing nucleic acid suitable for HPLC analysis is digestion with a restriction endonuclease , a procedure which, for relatively homogeneous DNA, generates a finite and often low number of well defined fragments (Column 13, lines 20-24)". An ordinary artisan would have been motivated by the express statement of Bloch et al to substitute and combine the model of restriction endonuclease digestion of Bloch et al with the methods of comparative hybridization and sequencing of Oefner et al. in order to achieve the express advantages, as noted by Bloch et al. , of a method which for relatively homogeneous DNA, generates a finite and often low number of well defined fragments.

9. Claims 1-3, 57-74, and 145-156 are rejected under 35 U.S.C. 103 (a) over Oefner et al. (U.S. Patent 5,795,976) (August 18, 1998) in view of Bloch et al (U.S. Patent 5,866,429) (February 2, 1999) further in view of Fox et al. (U.S. Patent 6,140,086) (October 31, 2000).

Oefner et al. in view of Bloch et al teach the method of claims 1-3, 57-74, and 145-155 as described above.

Oefner et al. in view of Bloch et al do not teach the method wherein the infrequently cleaving restriction endonuclease is selected from NotI.

Fox et al teach the method wherein the infrequently cleaving restriction endonuclease is selected from NotI (Column 17, lines 46-67).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine within the method of comparative hybridization and sequencing of Oefner et al in view of Bloch et al., the method of NotI restriction endonuclease digestion of Fox et al. since Fox et al state, "Restriction endonucleases that may be advantageously used in the methods of the invention include, but are not limited to AluI, Eco47 III, -- , NotI, PstI, PuvI, SacI/SstI, SalI, XbaI, XhoI and I-CeuI. Such restriction endonucleases are available commercially (Column 17, lines 57-64)". An ordinary artisan would have been motivated by the express statement of Fox et al to substitute and combine the method of NotI restriction endonuclease digestion of Fox et al. with the method of comparative hybridization and sequencing of Oefner et al in view of Bloch et al., in order to achieve the express advantages, as noted by Fox et al. , of a restriction endonuclease which may be advantageously used in the methods of cloning nucleic acid molecules and which are available commercially.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti , Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to

Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0195.

Arun kr. Chakrabarti

Arun Chakrabarti,

Patent Examiner,

February 22, 2001

JEFFREY FREDMAN
PRIMARY EXAMINER